SODIUM ISOAMYLETHYL BARBITURATE*

REPORT ON ITS USE AS AN AUXILIARY ANESTHETIC

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BARBITAL and the barbiturates have been known and used for many years, but it was not until 1929,[1] that sodium isoamylethyl barbiturate, after animal experimentation, was added to our list of auxiliary anesthetics for man.

At first, and in many places, it was tried for producing complete anesthesia. Because of its seriously depressing action on respiration and blood pressure and its prolongation of the period of unconsciousness, with its attendant disadvantages and dangers, we have never administered it in large doses that might jeopardize the patient, but merely as an adjunct to other anesthetics—as part of the preliminary medication.

A report following one hundred and fifty instances of its use at Stanford University Hospital has been given by Doctors Holman and Palmer.[2] Additional cases have been added to this list since then, but these will not be detailed at this time. It may be of interest to discuss our experience with it in general and also to review some of the salient features which were observed in various types of operations on patients who had received sodium isoamylethyl barbiturate.

PRELIMINARY NARCOSIS

At first we complied with the suggestion of ordering ephedrin, three-fourths or three-eighths grain, before the sodium amytal. After a short experience it was found that ephedrin was not necessary for the conservative doses of sodium amytal we gave and its use as a preliminary safeguard was discontinued. We keep it and caffein and a 10 per cent carbon dioxid-90 per cent oxygen mixture on hand at all times, to be given if needed.

A preliminary narcotic of morphin or morphin and atropin was found to be valuable for a smoother anesthesia resulted. This result is plausible when we consider that the barbitals affect the subcortical centers, while morphin has a cerebral-cortical action, as has been shown experimentally by Pick;[3] and scopolamin affects mainly the cord and central nervous system. Sodium isoamylethyl barbiturate affects the autonomic nerves and the subcortical areas and in large doses poisons skeletal and smooth muscle; in fact, acts as a general protoplasmic poison and depressant of metabolism.

Some patients received sodium isoamylethyl barbiturate by mouth. The action was slower and less profound than when given intravenously, but had the advantage of not introducing a foreign substance that could be given in some other manner into the blood stream.

Although many things about the drug are not as yet completely understood, it is known that it precipitates at the reaction of blood, which is PH 7.4, and therefore presumably intravenously, since sodium amytal is in solution in much higher degrees of alkalinity, namely, PH 9.5 to 9.8.[1,4] It is likely, therefore, that it exists in a colloidal of flocculent state in the blood.

PRECAUTIONS OBSERVED IN USE

Because of its possible untoward effects, both immediate and later, we introduced the solution very slowly when given intravenously, taking blood pressure constantly. If the blood pressure dropped suddenly or considerably (20 to 40 degrees) from the preliminary reading or if there was great depression of respiration, we either discontinued the injection altogether or if it seemed desirable to give a larger dose, we waited a minute or two for the blood pressure to improve before introducing more into the vein, and gave no more if the blood pressure continued to fall. At no time was it given faster than one cubic centimeter a minute and usually more slowly.

PHYSIOLOGIC REACTIONS TO DRUG

Blood pressure readings, pulse, and respiration were taken throughout the operation. In only a few instances was the respiration sufficiently depressed to require the addition of carbon dioxid. There was no occurrence of delirium when the drug was given, but several of those who had had larger amounts of around twenty grains showed some delirium after operation. This was calmed by morphin.

The amount of sodium amytal which was used, in most instances did not keep the patient quiet during the preparation of the skin. Nitrous oxid-oxygen was begun as soon as any restlessness or movement was shown. Patients were often sufficiently asleep, however, to make it advisable to use an airway, as the tongue tended to relax and drop back or at least block free breathing; but as the pharyngeal reflex was usually still somewhat active, the airway was not inserted as far as the pharynx.

During the anesthesia with nitrous oxid and oxygen following sodium isoamylethyl barbiturate the pupils were small or of moderate size, and the eyes were usually fixed and looking forward as in surgical anesthesia; whereas in nitrous oxid-oxygen anesthesia with preliminary medication of morphin or even scopolamin and morphin, the eyeballs ordinarily roll gently.

Even with moderate and small doses of sodium isoamylethyl barbiturate, the patients require more postoperative nursing care because of the longer period of unconsciousness, the occasional restlessness or delirium, and the necessity of clear-

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ing away any mucus which may be present and which, because of the slow return of reflexes, is in danger of being aspirated. Whether this mucus is more glairy than that of the average patient is, I believe, a disputed question. The same holds true of the incidence of postoperative pulmonary complications. Without due nursing care, especially after long duration of sleep or in patients who have a chronic cough, passive congestion and other untoward pulmonary and other conditions have been known to occur.[5]

When sodium amytal is used, an ideal dose would seem to be one which would send the patient into a light sleep either in his own room or in a pleasant anesthetic room; a dose that would not depress respiration or decrease blood pressure more than a slight initial drop, which would have recovered by the time the operation itself begins, or shortly after; and a dose that would require a nitrous oxid-oxygen anesthesia to be maintained during the preparation of the operative field and during the operation, and would leave the patient so lightly asleep at the close that he could be roused easily by speaking to him. This would offer most of the advantages of the drug without its dangers or disadvantages. This is the procedure which we are now following.

REPORT OF RESULTS

In giving our results with nitrous oxid and oxygen after sodium amytal, it must be borne in mind that for years nitrous oxid and oxygen has been our anesthetic of choice in a large percentage of our operative work. Our surgeons, almost without exception, have trained themselves to a gentle manner of operating, a feather touch, so essential to the best surgery and which does not require patients to be as profoundly asleep nor muscles as limp as some desire.

As a result, thyroidectomies, thoracoplasties, radical breast amputations, prostatectomies, herniaoplasties, and all bone or nerve surgery have for years been possible under nitrous oxid and oxygen, usually without ether or occasionally with the addition of a few breaths of it for greater relaxation; and without the amount of cyanosis or anoxemia described by many. Even stomach, gall gladder and like operations have quite frequently been performed without auxiliary ether.

As there has been very little or no vomiting as a rule after our routine anesthesias, we cannot, definitely, from our charts credit sodium isoamylethyl barbiturate with this advantage, though possibly there has been even less nausea than usual following it. We can say, however, that after sodium amytal we have not noticed any attempts on the part of patients to vomit during the nitrous oxid-oxygen anesthesia, as they will at times try to do during nitrous oxid-oxygen without the drug, to the inconvenience of the surgeon and the distress of the anesthetist.

Aside from any consideration of the toxic properties of the new drug, our results with its use as preliminary medication were in themselves very satisfactory. Some groups of cases may be of interest.

REPORT OF CASES

Five patients who had thoracoplasties varied in age from 17 to 45 years and in weight from 124 to 141 pounds. Morphin sulphate one-sixth grain and atrophin sulphate 1/150 was given in each case a half-hour before. Sodium amytal was introduced slowly intravenously, the doses being 6, 11, 12, 12 and 15 grains. No ether was used; 10 to 30 per cent oxygen was added to the nitrous oxid, averaging 20 per cent in most cases.

Fourteen thyroidectomies were performed after injecting the drug. The ages were from 26 to 61 years, and the weights from 95 to 152 pounds. Preliminary morphin, from one-eighth to one-fourth grain, but one-sixth in most cases was given with atropin. The sodium amytal used varied from 9 grains in five of the patients to 16½ grains in one patient. Only once was as little as 10 per cent oxygen used. The others received 15 to 35 per cent each, in many instances 20, 25, and 30 per cent for the greater part of the operation. No ether was used for any of these.

Ether was not used for the four patients with breast amputations, who each had morphin one-sixth and atropin 1/150; and who had sodium isoamylethyl barbiturate in doses of 6, 10, 13½, and 15 grains. Their ages varied from 37 to 67 years and their weights from 106 to 212 pounds. Oxygen given varied from 10 to 35 per cent, but was mostly 20 to 35 per cent.

Four gastro-enterostomy patients were satisfactorily relaxed with 9, 12, 13½, and 15 grains of sodium amytal, no ether being used. Oxygen varied from 10 to 25 per cent. Two others had to have a few breaths of ether to give sufficient relaxation. They had 9 and 12 grains of sodium amytal intravenously and 10 to 25 per cent of oxygen was used. Each of the six had morphin one-sixth and atropin 1/150 a half-hour before. So also did two patients for gastro-enterostomy and appendectomy who had 12 and 14 grains of sodium amytal and 5 to 25 per cent oxygen. One of these had a few breaths of ether at the start.

A resection of the stomach was performed without addition of ether on a 55-year-old patient receiving 6½ grains of the drug intravenously. Ten to twenty per cent oxygen was given with the nitrous oxid.

Four prostatectomy patients each had morphin one-sixth and atropin 1/150 followed in an hour by sodium amytal 7, 7½, 7½, and 9 grains, respectively. They were satisfactorily relaxed without ether on a nitrous oxid anesthesia with 15 to 25 per cent oxygen.

Six patients who had rectal work, as fistula in ano, rectal polyp, hemorrhoids, and prolapse of rectum, received sodium isoamylethyl barbiturate in doses varying from 9 to 20 grains, following morphin one-sixth and atropin 1/150 in all except two, who received morphin one-fourth. They remained relaxed without ether and with the use of nitrous oxid with 10 to 30 per cent oxygen added.

Three patients had operations on the liver, one for carcinoma, and two for abscesses. They received as preliminary preparation, morphin sulphate grains one-sixth with atropin 1/150, and 6, 9, and 10 grains of sodium isoamylethyl barbiturate intravenously. No ether was required in any, but nitrous oxid was given with 15 to 25 per cent oxygen.

To mention the five operations on gall bladders, thirteen hernias, and many other operations done in like manner would seem like repeating the same story under different names.

COMMENTS

At no time did we have a serious initial fall in blood pressure or a marked later fall that could be blamed on the drug. There was usually a fall about the time the patient lost consciousness which

returned almost to normal near the start of the operation.

There were a few instances of depressed respiration which were readily improved by the addition of carbon dioxid.

CONCLUSIONS

In the preliminary preparation, the addition of a small or moderate dose of sodium isoamylethyl barbiturate has made it easier to keep patients properly relaxed; has, so to speak, broadened the plane or region in which they remain satisfactorily asleep.

It has made possible on most occasions the administration of a larger amount of oxygen than usual.

Ether has had to be added to the nitrous oxid anesthesia in fewer instances.

It has relieved nervous and apprehensive patients of the realization that they will receive an inhalation anesthesia which they have dreaded.

There has been less nausea and vomiting.

The patient did not awake sufficiently to become unpleasantly sensitive to the return trip to his room.

Opposed to these advantages is the objection raised against introducing a foreign substance intravenously, when it can be prevented.

If the small or moderate doses now recommenced are not exceeded, and if the usual precautions are taken after operation, there is not likely to be postanesthetic delirium, or dropping of the tongue, or the long relaxed sleep with the hazards it favors, unless extraordinary precautions are taken to prevent them.

Nursing care will be somewhat increased, but not markedly so, if moderate amounts only are used.

If properly administered in selected cases, sodium isoamylethyl barbiturate may be considered a useful addition to our anesthetic armamentarium.

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CHEMICAL ADJUNCTS TO GENERAL ANESTHESIA*

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CHEMICAL adjuncts to general anesthesia were introduced with Claude Bernard's suggestion (1869) that morphin be given before anesthesia to relieve fear and worry and to make anesthetization easier. Chemical agents are now indicated as adjuncts to general anesthesia for many other purposes besides (*a*) preanesthetic hypnosis, as (*b*) the regulation of metabolism preoperatively, (*c*) for aid in the induction, maintenance, and rapid recovery from direct anesthesia, (*d*) for the relief of postanesthetic nausea, and (*e*) for postoperative analgesia.

PREANESTHETIC HYPNOSIS

The chief object of using chemical agents as preanesthetic hypnotics is to relieve the fear most patients have of the coming operation and particularly of the administration of the anesthetic. While this fear may be alleviated by proper psychic preparation of the patient, the preanesthetic hypnotic is also useful in lowering the patient's general metabolic level to a point where the anesthetic itself may be easily and smoothly administered. Then a proper depth of surgical anesthesia may be readily obtained by nitrous oxid and oxygen without pushing the nitrous oxid to dangerous asphyxial concentrations. This is well recognized to be the safest and most easily controlled general anesthetic, avoiding the severe metabolic disturbances caused by ether or chloroform and the explosive risk of ethylen.

In spite of the fact that there is great dissatisfaction with morphin and hyoscin (scopolamin) as preanesthetic hypnotics, they continue in general use in the absence of any pressing clinical necessity for something better. This is surprising in view of their definite and independent condemnation years ago by such competent clinical observers as Herb, Gatch, and Bevan.[1] A consideration of the pharmacology of these agents may be of interest in support of this clinical opinion.

Morphin primarily causes a general stimulation of the central nervous system, which is promptly masked in humans by a secondary depression. But *the stimulating action outlasts the depression.* This leads to increased irritability and cortical excitement after the depression wears off, and is apparently responsible for the initiation of the craving and habit (to get back again the pleasant euphoria of the depressant stage).[2] Morphin is further not helpful in anesthesia because the tendency to respiratory depression interferes with the rapidity of absorption or elimination of an inhalation anesthetic, and its tendency to cause con-

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